

Original Article

Therapeutic effect of ceftriaxone and penicillin g procaine in patients with early-stage syphilis

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Abstract: Objective: To compare the therapeutic effect of ceftriaxone sodium and penicillin G procaine in patients with early-stage syphilis, so as to provide guidance for clinical treatment of early-stage syphilis. Methods: 60 early-stage syphilis patients who were receiving syphilis treatments in our hospital were enrolled and assigned into ceftriaxone group (n=30) and penicillin G procaine group (n=30) by using a random number table. Ceftriaxone sodium or penicillin G procaine therapies were applied to the corresponding group respectively. The subsidence rate of skin lesion was detected and compared one week after treatment, while the negative rate of TRUST test and serum complement fixation rate were detected and compared at 1, 3, 6, 9, and 12 months after treatment. Results: Patients in the ceftriaxone group showed a much higher subsidence rate of skin lesion than the penicillin G procaine group after 1 week ($P<0.05$); no statistical significant difference was observed in the negative rate of TRUST at 3, 6, 9, and 12 months after treatment between two groups ($P>0.05$), and no statistical significant difference was observed in the serum complement fixation rate at 1, 3, 6, 9, and 12 months after treatment between two groups ($P>0.05$) as well. Conclusion: Our study demonstrated a comparable clinical efficacy of ceftriaxone and penicillin G procaine for early-stage syphilis.

Keywords: Early-stage syphilis, ceftriaxone, procaine penicillin

Introduction

In recent years, an increase of outpatient visits by patients with early stage syphilis was observed in STD clinic. The incidence rate of syphilis is rising rapidly in China recently [1]. By far, penicillin is the first-line medicine for early-stage syphilis. However, it is far from sufficient due to the long-term low serum negative rate and high serum complement fixation rate [2]. Literature has confirmed ceftriaxone to be a potential anti-syphilis drug by reducing the serum fixation rate effectively in patients with early stage syphilis [3]. To compare the therapeutic effect of ceftriaxone and penicillin G procaine, we selected and grouped 60 early-stage syphilis patients who were receiving syphilis treatments in our hospital, and treated each group with ceftriaxone or penicillin G procaine correspondingly, and the results are as follows.

Materials and method

General information

Sixty patients with early syphilis treated at our hospital from May 2014 to May 2015 were selected according to the following inclusion criteria: (1) conformed to diagnostic criteria for early syphilis; (2) negative for HIV; (3) signed informed consent with good compliance; (4) not having received medication. The patients were excluded if any of the following exclusion criteria was met: (1) combined with low immunity; (2) diagnosed as tumors; (3) concurrent with severe diseases of liver, heart and kidney; (4) women during lactation or pregnancy. Random number table was used to divide 60 patients into ceftriaxone (CTR) group (n=30) and penicillin G procaine group (n=30). CTR group consisted of 16 males and 14 females, aged 22-67 years (average, 35.4 ± 9.5 years). They were classified into primary syphilis (12 cases), sec-

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Table 1. Comparison of subsidence of skin lesions between the two groups within 1 week

Group	Total number of cases	Number of cases achieving subsidence of skin lesions	Number of cases not achieving subsidence of skin lesions	Subsidence rate
CTRX group	30	27	3	90.00%
Penicillin G procaine	30	20	10	66.67%
χ^2 value			4.812	
<i>P</i> value			0.028	

Table 2. Comparison of negative conversion rate in trust

Group	1 month [n (%)]	3 months [n (%)]	6 months [n (%)]	9 months [n (%)]	12 months [n (%)]
CTRX group	6 (20.00)	13 (43.33)	23 (76.67)	28 (93.33)	30 (100.00)
Penicillin G procaine group	1 (3.33)	7 (23.33)	18 (60.00)	25 (83.33)	28 (93.33)
χ^2 value	4.043	2.700	1.926	1.456	2.069
<i>P</i> value	0.044	0.100	0.165	0.228	0.150

ondary syphilis (13 cases) and early latent syphilis (5 cases), Penicillin G procaine group consisted of 14 males and 16 females, aged 23-68 years (average, 34.6±9.4 years). They were classified into primary syphilis (14 cases), secondary syphilis (12 cases) and early latent syphilis (4 cases). The two groups did not differ significantly in age, gender and syphilis classification ($P>0.05$).

Treatment

For CTRX group, intravenous infusion of 1.0 g CTRX was performed once daily for 10 days. For penicillin G procaine group, intramuscular injection of 800,000 units penicillin G procaine was performed once daily for 15 days.

Indicators

The patients were followed up for 12 months and received toluidine red unheated serum test (TRUST) 1 month, 3 months, 6 months, 9 months and 12 months after treatment, respectively, in accordance with the manufacturer's instructions. The treatment effect was evaluated by subsidence of skin lesions and serologic test. Absence of clinical and serologic evidence of progression of syphilis during follow-up was considered successful treatment.

Statistical process

Statistical analysis was performed using SPSS21.0 software, the data were expressed as mean ± standard deviation, and the means

of the two groups were compared by *t*-test. The count data of the two groups were compared by *Chi*-square test, and $P<0.05$ indicated statistically significant difference.

Results

Comparison of subsidence of skin lesion between the two groups after treatment for 1 week

In CTRX group, 27 patients achieved subsidence of skin lesions within 1 week with subsidence rate of 90.00%; in penicillin G procaine group, 20 patients achieved subsidence of skin lesions within 1 week, with subsidence rate of 66.67%. The subsidence rate of CTRX group was significantly higher than that of penicillin G procaine group ($P<0.05$) (**Table 1**).

Comparison of negative conversion rate in TRUST between the two groups at different time after treatment

The negative conversion rate in TRUST of CTRX group was significantly higher than that of penicillin G procaine group at 1 month after treatment ($P<0.05$). However, at 3 months, 6 months, 9 months and 12 months after treatment, the two groups did not differ significantly in negative conversion rate in TRUST ($P>0.05$) (**Table 2**).

Comparison of incidence of sero-resistance between the two groups

After the manifestations had disappeared for 6 months, serum positive for unheated serum

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Table 3. Comparison of incidence of sero-resistance between the two groups

Group	Total number of cases	Number of cases with sero-resistance	Incidence of sero-resistance
CTRX group	30	5	16.67%
Penicillin G procaine group	30	7	23.33%
χ^2 value		0.417	
P value		0.519	

reagin test was defined as sero-resistance. Five patients in CTRX group had sero-resistance, and 7 patients in penicillin G procaine group had sero-resistance. The two groups did not differ significantly in incidence of sero-resistance ($P>0.05$) (Table 3).

Discussion

Syphilis is a chronic, systematic sexually transmitted disease caused by *Treponema pallidum*, which has four stages (primary, secondary, tertiary, and latent stage). Syphilis can be also congenital (prenatal syphilis) [4]. The patients affected by syphilis can have *Treponema pallidum* in skins and mucosa, which can be transmitted via sexual contact if skin or mucosa has a small cut. Very few cases are infected by blood transfusion or other routes. Early acquired syphilis is transmitted by risky or unprotected sexual contact for over 95% of the patients, and very few get infected by kissing, blood transfusion and contact with the polluted clothes [5]. Prenatal syphilis is transmitted from mother to fetus. Pregnant women having primary, secondary and early latent syphilis are associated with a very high probability of transmitting syphilis to fetus. Syphilis can involve nearly every organ of the human body [8]. Syphilis is both physically and psychologically debilitating. Syphilis patients are usually the victims of social discrimination and bring harm to their families. The incidence of syphilis is rising in China every year. A recent report on syphilis indicates that syphilis now ranks the third among the category A and B infectious diseases in China. The manifestations of primary syphilis include genital ulceration. As a large number of *Treponema pallidum* enters the blood circulation after 6-8 weeks, the patients will suffer from skin lesions accompanied by low fever, physical discomfort and lymph node swelling, which are the symptoms of secondary

syphilis [7]. At this stage, the immune responses are activated, and *Treponema pallidum* is killed in large quantities. Thus the symptoms will be alleviated or disappear. However, the residual *Treponema pallidum* may upset the immunity and enter the blood circulation, attacking the central nervous system and cardiovascular system [8]. There-

fore, effective treatment of early syphilis is of high importance.

The first-line treatment for syphilis is intramuscular injection of penicillin. Penicillin G procaine and penicillin G benzathine are the most common drugs, while CTRX is the second-line drug for treating neurosyphilis. Penicillin is considered the most effective drug against syphilis so far. After intramuscular injection, the effective concentration of penicillin in blood can be maintained for about 1 week. Besides the advantages of easy use and low cost, no penicillin-resistant strains have been reported in syphilis patients so far [9]. However, penicillin injected intramuscularly under the recommended dose may have poor penetration across the blood-brain barrier (BBB), thereby failing to achieve a stable concentration in cerebrospinal fluid (CSF) necessary to kill *Treponema pallidum* [10]. Study has shown that CTRX displays excellent inhibitory activity on *Treponema pallidum* outside the cells *in vivo*. CTRX works by inhibiting the cell wall synthesis of *Treponema pallidum* and thus inhibiting the proliferation of *Treponema pallidum*. CTRX has a poor affinity with plasma proteins, and the free CTRX will accumulate and enter the tissues and organs [11]. CTRX administered at conventional dose can penetrate across BBB and enter CSF. This drug has longer serum half-life, high bioavailability and safety [12].

In this study, the subsidence rate of skin lesions within 1 week of treatment was significantly higher in CTRX group than in penicillin G procaine group ($P<0.05$). At 1 month after treatment, the negative conversion rate in TRUST in CTRX group was considerably higher than in penicillin G procaine group ($P<0.05$). This is probably because CTRX has a longer half-life and thus can persistently kill *Treponema pallidum* at the conventional dose. At 3 months, 6

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months, 9 months and 12 months after treatment, the negative conversion rate in TRUST did not show significant difference between the two groups ($P>0.05$); the incidence of seroresistance was not significantly different between the two groups either ($P>0.05$). This indicated that the two groups had comparable effect in treating early syphilis.

Disclosure of conflict of interest

None.

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